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Occupational Exposure to Chlorinated Aliphatic Hydrocarbons: Job Exposure Matrix

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A job exposure matrix combining features to increase the accuracy of exposure assessment was developed to evaluate cancer risks from workplace exposures to six chlorinated aliphatic hydrocarbons (CAHs). A detailed description of the matrix is provided to satisfy the need for more in-depth discussion of exposure assessment methods than is typical in today's epidemiologic literature. The matrix assigns semiquantitative estimates of the probability and intensity of exposure to each four-digit Standard Industrial Classification (SIC) and Standard Occupational Classification (SOC) code potentially associated with exposure to each CAH. The matrix also accounts for the changing patterns of use of the CAHs by decade from the 1920s to the 1980s. An algorithm combines these parameters to assign each study subject a unique lifetime probability of exposure and an estimated score of cumulative exposure for each CAH. These assignments can then become the subjects of analyses. The ability of the matrix to reduce the number of false positive exposure assessments is discussed and illustrated. A companion paper describes the detailed epidemiologic findings of this application of the matrix.

Key words: exposure assessment methods, chlorinated solvents, SIC, SOC, false positive exposure assessments

INTRODUCTION

Since their introduction in the early 1900s, chlorinated aliphatic hydrocarbons (CAHs) have found widespread use in industry and commerce because of their versatile properties. As a result, occupational exposures to these compounds have occurred in disparate kinds of workplaces, including the chemical, agricultural, food and paint industries, the manufacture of metal, plastic, and electronic goods, hospitals, dry cleaning establishments, and beauty shops. The popularity of individual compounds in the group has varied over time, and continues to vary today, in response to changing economic, technologic, and toxicologic realities. These factors have produced an intricate history of potential occupational exposure to this group of

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chemicals. In the early 1900s, for example, tetrachloroethane and carbon tetrachloride were the most commonly used CAHs. In part because of workplace intoxications with these two substances, however, they were gradually replaced in many uses by trichloroethylene and tetrachloroethylene. In mid-century, methylene chloride (dichloromethane) and methyl chloroform (1,1,1 trichloroethane) began replacing the two ethylenes in many applications [Hoar et al., 1985; Center for Chemical Hazard Assessment, 1985a,b,c,d], although methylene chloride has apparently been declining in popularity in the more recent past.

Because of their widespread use and the resulting human exposures, these CAHs have come under considerable toxicologic and regulatory scrutiny [NIOSH; IARC, 1979, 1986, 1987]. The carcinogenic and mutagenic properties of six of the most common and important members of this group of chemicals (carbon tetrachloride, chloroform, methylene chloride, trichloroethylene, methyl chloroform, and tetrachloroethylene) have been reviewed by the International Agency for Research on Cancer [IARC, 1979, 1986, 1987]. All except methyl chloroform were carcinogenic in animal bioassays and four were mutagenic. Epidemiologic investigations also suggest that some of these CAHs may be human carcinogens, but many of the cohort studies are based on small populations, and the exposure assessment underlying the case-control studies has been weak [IARC, 1986, 1987; Blair et al., 1980; Hearne et al., 1987; Axelson, 1980; Lanes et al., 1990].

It is difficult to assemble cohorts of workers with well-defined exposures to any single one of these substances, and the complex use patterns over the last decades also make these substances extremely difficult to investigate through case-control studies. Epidemiologic studies are needed, however, to evaluate their potential carcinogenicity. In order for such studies to be successful, however, there is a critical need to develop *exposure assessment methods* that can account for the complexity of past exposure patterns to these CAHs more effectively than has been the case until now. Yet such methods receive scant attention in epidemiologic research reports, typically a few pithy sentences describing a "black-box" type of process, with little detailed description or critical commentary, despite their key role in the elucidation of risks.

One exposure assessment approach that may at times be effective is the use of a job exposure matrix. This approach may increase power by grouping workers with similar exposures in different industries and thus reducing the dilution of relative risks due to nondifferential misclassification [Hoar et al., 1980; Hoar, 1984; Acheson, 1982]. If a matrix has better discriminating power in assessing exposures than methods where analyses are based, say, on individual job titles, and a true exposure-disease relationship exists, then the application of the matrix should result in stronger measures of association and more confidence in their interpretation [Stewart and Herrick, 1991].

The purpose of this report is to describe a job exposure matrix which was developed for the six chemicals listed in Table I, to discuss its strengths and weaknesses, and to illustrate them by summarizing some results of its application to the data from a case-control study of astrocytic brain tumors. The detailed methodologic description explicitly seeks to stimulate more in-depth review and discussion of exposure assessment methods than the cursory descriptions typically found in today's literature.

As described in the next section, the matrix incorporates concepts of probability and intensity of exposure that are intended to overcome difficulties in retrospective

TABLE I. Bioassay Carcinogenicity and Mutagenicity of Six Chlorinated Aliphatic Hydrocarbons (CAHs)*

Chlorinated hydrocarbon	Bioassay carcinogenicity	Mutagenicity
Carbon tetrachloride	+	−
Chloroform	+	−
Methylene chloride	+	+
Methyl chloroform	−	+
Trichloroethylene	+	+
Tetrachloroethylene	+	?

*+ = positive; − = negative; ? = inconsistent results. (Data from IARC Monogr, Vol. 20, 41, Suppl. 7.)

exposure assessment in case-control studies. Although these features are not new, they have only rarely been used in case-control studies. They have also not been used in the same manner in a job exposure matrix, or described critically in the literature. An assignment of level of exposure by year was applied in a nested case-control study of liver angiosarcoma [Greenberg and Tamburro, 1982]. Calendar years of use have appeared in other exposure assessments [Stewart et al., 1986], and time was considered as a factor in a job exposure matrix in a case-control study of non-Hodgkin's lymphoma (NHL) [Blair et al., 1992]. Trends by probability of exposure to lung carcinogens were previously evaluated [Kjüs et al., 1986], and the concept of probability of exposure has also been used in an algorithm for calculating cumulative exposures [Siemiatycki et al., 1988].

MATERIALS AND METHODS

A job exposure matrix was developed to estimate exposures to six CAHs among the white male subjects of a case-control study of astrocytic brain cancer.[1] The study subjects died in Lousiana, New Jersey, and Pennsylvania between 1978–1981, and the details of the original data collection and study can be found elsewhere [Thomas et al., 1987]. The epidemiologic findings from the application of the matrix to a portion of the original data are reported in a companion paper [Heineman et al., 1994].

The matrix was designed to use the available information about the work histories of all the study subjects in such a way as to minimize misclassification by reducing the number of false positive exposure assessments. The next of kin of cases and controls had originally been interviewed with a standard questionnaire to collect occupational histories and information about other risk factors. For our investigation, all the jobs reported in the original work histories were coded for four-digit Standard Industrial Classification (SIC) [Office of Management and Budget, 1972] and Standard Occupational Classification (SOC) [U.S. Department of Commerce, 1977] codes, because the matrix is based on these coding systems.

As described in more detail below, the application of the matrix to the coded job

[1]Throughout this paper, the word *exposure* signifies *potential exposure*, since no direct measures of exposure were available.

histories resulted in the assignment of a unique probability and intensity of exposure for each study subject and each of the six CAHs. Exposures (yes/no) were assigned by decade (1920s–1980s) to account for changing patterns of use of the chemicals over time. The matrix weighted the available information from industry and occupation to emphasize that which was more informative about potential exposure. An algorithm combined the probabilities and intensities assigned by the matrix with duration of exposure to calculate a cumulative exposure score as a surrogate of dose and as a tool for analysis.

Probability and Intensity Scales of Occupation and Industry Codes

In the matrix, each four-digit SIC and SOC code potentially associated with exposure to each of the CAHs under study was assigned values for semiquantitative estimates of the probability (low, medium, and high) and the intensity (1,2,3) of exposure. These values were assigned a priori to all SIC and SOC codes; they were not based on the work history data. The intensity scale should be interpreted as an average measure of exposure that reflects both the concentration of exposure and the frequency. The two scales allow the development of an algorithm weighting the available information from industry and occupation, which is described below. They are meaningful only in relative terms, however, because they do not reflect absolute scales of measurement, and they are not comparable across CAHs in any quantitative sense. The development of the matrix and the coding of the work history data were carried out without knowledge of the case or control status of the subjects.

In a few instances, new occupational codes were introduced to capture exposure-related information which would have been lost with the use of the existing SOC categories. Examples are new codes for the jobs of surgeon and anesthesiologist, which in some periods entail possible exposures to chloroform. The existing SOC categories only allowed coding as physician, which would have meant a loss of exposure-related information, since most physicians have not been occupationally exposed to any CAHs.

Weighting of Occupation and Industry Information

Because occupational codes often implicitly convey information regarding exposures, they played an important role in the decisions leading to the assignment of a unique probability and intensity of exposure to each occupation-industry combination. For example, the code for dry cleaning machine operators clearly indicates exposures to several of the CAHs considered in this study, depending on the time period, since carbon tetrachloride, trichloroethylene, and tetrachloroethylene have all been used extensively in dry cleaning. In order to take advantage of the information implicit in such job titles, occupational codes were assigned to one of three categories, reflecting the varying specificity of information about exposure implicit in them.

Category A. Occupational codes assigned to this category were those sufficiently informative to assess the potential for exposure, independent of the industry where the job was performed. For example, a printer was considered to have the same probability and intensity of exposure to several of the CAHs, no matter whether the subject worked as a printer in a printing-related industry, such as newspapers, or in a school or the armed services. A dry cleaner operator is another example, because the exposure depends primarily on the characteristic tasks of the occupation, and not the industry where they are performed. In occupation-industry combinations with this

TABLE II. Algorithm for Calculation of Cumulative Exposure Scores for Different Job-Industry Combinations*

Occupational category	Probability of exposure in the industry	Cumulative exposure algorithm (duration × intensity^2)	Rationale
A	Any	DUR × E_0^2	Intensity fully determined by job
B	Low	DUR × $(E_0^2 \times E_i)^{2/3}$	Occupation intensity weighted more
	Medium	DUR × $(E_0 \times E_i)$	Occupation and Industry intensities weighted equally
	High	DUR × $(E_0 \times E_i^2)^{2/3}$	Industry intensity weighted more
C	Any	DUR × E_i^2	Intensity fully determined by industry

*E_0, estimate of intensity of exposure for occupational code (SOC); E_i, estimate of intensity of exposure for the industry (SIC); DUR, duration of exposure in years.

type of code, both the probability and intensity of exposure were determined only by the values assigned to the occupational code.

Category B. Occupational codes assigned to this category were those in which the probability of exposure depended solely on the industry. The intensity of exposure assigned to these codes, on the other hand, was weighted by *both* the occupation and the industry. For example, in an industry where a given CAH was used, the matrix assigns a manager and an assembler the same probability of exposure, but a lower intensity to the manager.

Category C. This category applied only to situations where the information in the occupational code was missing or was so general that it was insufficient to assign one of the above categories. In these instances, which were very few, both the probability and the intensity of exposure were determined completely by the industry code. Examples are the codes for "occupation not specified" and "miscellaneous manual occupation."

Decade Indicators

The matrix accounts for the different time periods when the CAHs were in use in different industries and occupations. Based on information from a wide range of sources and their own expertise, the investigators assigned decade indicators (exposed, unexposed) according to the likely use of a CAH for a given application (e.g., degreasing or anesthesia) for each decade between the 1920s and the 1980s. Decade indicators were assigned to all SOC codes in Category A, where the occupation alone determined the probability of exposure, and to all SIC codes. Thus, if a worker was employed during a decade when a given substance was not yet or no longer used for a particular application in a given industry or occupation, the decade indicator and thus the matrix classified that person as unexposed for that period.

Algorithm for Cumulative Exposure

An algorithm was designed to combine the decade indicators, the probability and intensity estimates, and the duration of exposure into parameters amenable to epidemiologic analyses (Table II).

In the first step of the algorithm, each occupation-industry combination with a positive decade indicator in the work history of each study subject was assigned a unique probability of exposure (low, medium, high) and a unique intensity of exposure. In Category A jobs, the occupation defines all the needed parameters, i.e., the decade indicator, the probability and the intensity, because these are jobs where the exposures were considered to be the same across all industries, as described earlier. In Category B and C jobs, the industry alone determined the decade indicators and the probabilities, while the intensity was drawn from both occupational and industry information (Category B), or from the industry alone (Category C), as described below.

An exposure score was calculated for each job by multiplying the duration of exposure in years by a squared term representing the intensity of exposure in the job alone, in the job and the industry, or in the industry alone. Table II displays the formulas used to calculate the exposure scores and illustrates how the squared terms for intensity are derived for each job category. In Category A jobs, the intensity term was simply the square of the intensity value assigned for the job. In Category B jobs, the values for intensity from the industry and/or occupation were combined to obtain an equivalent squared term. The intensity values chosen for these combinations depended on the probability of exposure. By squaring the value for intensity (1,2, or 3) from industry and/or job and then taking the appropriate root, this scheme allows the matrix to emphasize the information from the occupation or the industry, as appropriate. The rationale is that when the probability of exposure in a particular industry is high, the intensity of exposure of the industry should weigh more in the estimation of the cumulative exposure score, hence the industry intensity is squared in the formula [Dosemeci et al., 1989]. In contrast, when the industry probability is low, the intensity of exposure in the occupation is emphasized by squaring it.

The squared form of the intensity term also expands the scale of exposure intensities to a ratio of 1:9 between the lowest and the highest intensity categories. In the absence of industrial hygiene data to define a "true" scale, this ratio is more reasonable than the ratio of 1:3 which would have resulted from the raw (linear) intensity assignment, and also more consistent with empirically observed distributions of exposure intensities [Esmen and Hammad, 1977; Dosemeci et al., 1989; Kromhout et al., 1987].

The final step in the algorithm simply sums the scores for all the occupation-industry combinations in each subject's work history to calculate a cumulative exposure score for a specific CAH. For the epidemiologic analyses, subjects with multiple probabilities in their work histories were assigned to the highest probability achieved.

RESULTS

Figure 1 displays the change in the number of SIC codes in the study data which were identified by the matrix as having exposure to each CAH over nearly six decades. Figure 1 includes all the probabilities of exposure and is thus the most sensitive form of the matrix, but similar patterns were found when only the high probability industries were examined. Four of the six CAHs evaluated in the study showed an increase in the *number of industries* where they were used since the early 1930s through the 1980s. Carbon tetrachloride and chloroform are the exceptions.

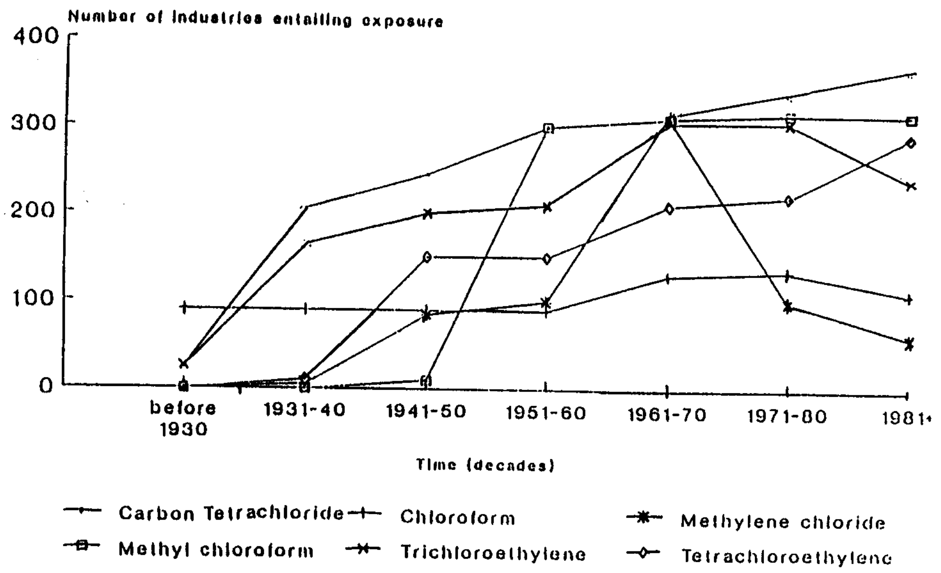

Fig. 1. Number of industries in the data classified as entailing exposures to six CAHs.

Carbon tetrachloride increased until the 1950s and then showed a substantial decline, while chloroform showed a rather constant diversity of use with only a small increase in the 1960s and 1970s. Figure 1 further illustrates that different CAHs began relatively widespread use at different times. Before the 1930s, for example, only carbon tetrachloride, trichloroethylene, and chloroform were widely used in many industries. Methylene chloride and tetrachloroethylene followed after the 1930s, while methyl chloroform only began to be used widely after the 1940s.

While Figure 1 displays the time of introduction and one measure of the diversity of use of the six CAHs, it does not illustrate the changes in the specific industries (SIC codes) where the CAHs were used over time, which is another important feature of the matrix. For example, the pattern of chloroform use by number of SIC codes in Figure 1 is relatively flat over the period of the study, possibly suggesting that the uses of this CAH remained unchanged during that period. This was not the case, however. The industries where chloroform was commonly used until the 1940s were quite different from those in the latter periods. For example, chloroform was a widely used anesthetic agent in the first half of the century, but it was largely substituted in that application by other substances after that time.

Figure 2 compares the frequency with which SIC codes were assigned exposure to multiple agents with and without the use of decade indicators. It illustrates the increase in specificity of exposure assignment resulting from the calendar-period feature of the matrix. The bars compare the proportions of SIC codes designated with exposure to one or more of the CAHs (up to a maximum of six possible concurrent exposures) resulting from application of the matrix (shaded bars) to the proportions which would have resulted from assignment without decade specificity (light bars). The proportion of SICs to which the matrix assigned concurrent exposure to five or six agents was reduced and, conversely, the proportion to which four or fewer exposures were assigned increased. The assignments with decade indicators thus

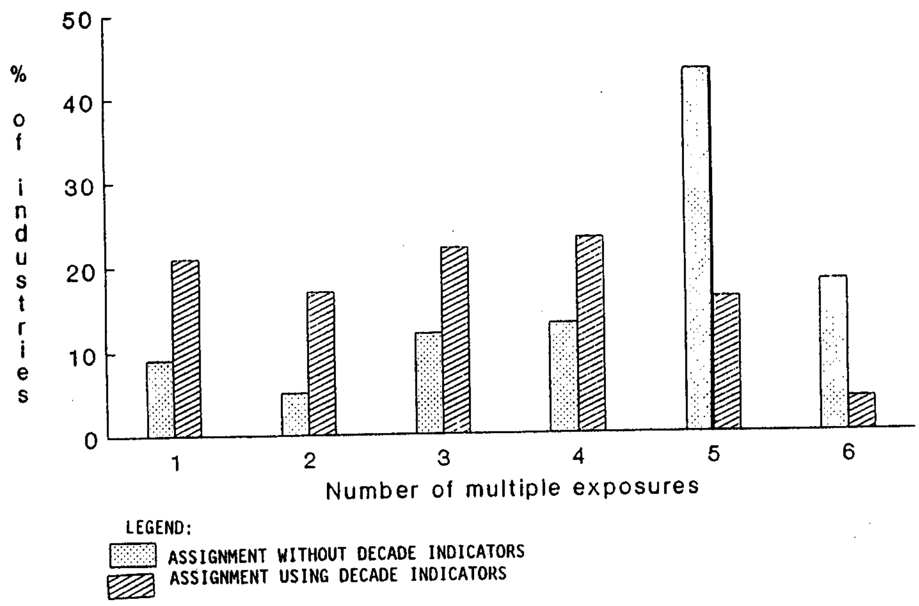

Fig. 2. Proportion of industries (SIC codes) with multiple exposures to six CAHs with and without decade indicators.

provided more opportunity to disentangle the effects of specific chemicals by reducing the number of instances where multiple exposures might have been incorrectly assessed.

As an example, Table III illustrates the influence of the decade indicators for exposure to methylene chloride in an individual work history. The history includes four jobs. The earliest job was in an industry where no CAHs were used in any decade, so the matrix classifies it as unexposed. The subject's second job was in a plant manufacturing ball and roller bearings, where methylene chloride was possibly used for metal cleaning only after 1960. The subject worked in that industry before the introduction of the CAH for that application, however, and was thus considered unexposed. In this instance, a static assignment without the decade indicators would have classified this as an exposed job. The third job is unexposed for all decades. The last job also involved an industry group, electronic component manufacture, where methylene chloride was introduced as a cleaning and process solvent in the 1960s. Because the employment occurred after that time, this job was therefore considered exposed.

Table IV illustrates the calculation of the cumulative exposure score to methylene chloride for the work history of the study subject in Table III. The first three jobs involved from 3–7 years in unexposed industries (negative decade indicators). These jobs did not contribute to the cumulative score. The last job involved 10 years considered unexposed (1951–1960), followed by 17 years over two decades with positive indicators (1961–1977). They contributed to the score according to the formulation illustrated in Table II. The occupation was in Category B, so that the probability of exposure in the industry determined how to combine the information

TABLE III. Application of the Job/Exposure Matrix for Methylene Chloride to a Sample Work History*

Job no.	Job category	Job dates (19__)	SOC	E_0	SIC	p	E_i	Years of work by decades (indicator[a]) <30	31–40	41–50	51–60	61–70	71–80	80+
1	Unexposed	35–42	7652 (Machine operator)	–	2252 (Textile)	Unexposed		0(–)	5(–)	2(–)	0(–)	0(–)	0(–)	0(–)
2	B	42–45	7720 (Assembler)	3	3562 (Carpentry)	L	2	0(–)	9(–)	3(–)	0(–)	0(+)	0(+)	0(+)
3	Unexposed	45–50	6122 (Carpenter)	–	1751 (Carpentry)	Unexposed		0(–)	0(–)	5(–)	0(–)	0(–)	0(–)	0(–)
4	B	50–77	83B0 (Machine cleaner)	3	3679 (Electronic)	H	3	0(–)	0(–)	0(–)	0(–)	10(+)	7(+)	0(–)

*, probability of exposure (H, high; L, low); E_0, intensity of exposure assigned to the occupation; E_1, intensity of exposure assigned to the industry. SOC, Standard Occupational Classification; SIC, Standard Industrial Classification.
[a]A positive (+) decade indicator identifies use of the chemical and resulting exposure in that decade. A negative (–) indicator means no use.

TABLE IV. Sample Calculation of Cumulative Exposure Score for Work History Illustrated in Table III

Job no.	Years on job	Decade indicator[a]	Cumulative exposure score calculation	Cumulative exposure score	Probability of exposure in industry
1	7	–	$[7 \times 0]$	0	0
2	3	–	$[3 \times 0]$	0	0
3	5	–	$[3 \times 0]$	0	0
4	17	+	$[(10 \times 0) + 17\,(3 \times 3^2)^{2/3}]$	153	High
Cumulative exposure score: 153					

[a]A + decade indicator identifies use of the chemical and resulting exposure in the appropriate decade. A – indicator means no use or exposure.

about intensity from industry and occupation. In this instance, the industry and occupational intensities are the same, so that, arithmetically, there was no practical differential weighting. The intensities of exposure for both industry and occupation were handled arithmetically as illustrated in Table II (for a Category B job and a high probability industry) and the result is multiplied by the duration of exposure (17 years) for a cumulative score of 153. Because the highest probability job for this subject was high, he was always included in the high probability subgroup in analyses.

Table V shows the proportion of study subjects exposed to each CAH by probability of exposure. The relatively high proportions in the low and medium probability categories indicate that the matrix is highly sensitive but probably not very specific when using these categories.

Finally, a modest effort was made to validate a small number of the exposure assignments, by trying to obtain additional information about 10 job-industry com-

TABLE V. Percentage Distribution of the Study Population by Probability of Exposure to Chlorinated Aliphatic Hydrocarbons (CAHs)

	Probability of exposure[a]			
CAH	Unexposed (%)	Low (%)	Medium (%)	High (%)
Carbon tetrachloride	58	33	4	5
Chloroform	85	11	3	1
Methylene chloride	62	24	9	5
Methyl chloroform	66	31	3	1
Tetrachloroethylene	65	22	10	4
Trichloroethylene	59	20	16	5

[a]Percentages rounded off to the nearest figure.

binations which were assigned a high probability of exposure to methylene chloride by the matrix. Unfortunately, the effort was not very rewarding. Five of the workplaces were no longer in business, three refused to provide information, and two could not identify individuals to comment regarding exposures many years in the past.

DISCUSSION

This report describes a job exposure matrix that combines several features intended to increase the accuracy of exposure assessment to six CAHs. These features were estimates of probability and intensity of exposures, and assignment of exposures by decades to account for changing patterns of chemical use. The rationale of the matrix and the results of its application, as reported in this paper and elsewhere [Dosemeci et al., 1993; Heineman et al., 1994], suggest that these approaches may reduce misclassification and thus improve the ability to identify an excess risk. The choice of a job exposure matrix for exposure assessment in a case-control study, however, and the specific characteristics and rationale of the matrix and algorithm described in this paper raise a number of important methodologic issues.

The most important issue is that our matrix cannot claim to be an exception to the rule that no currently available or foreseeable method of retrospective exposure assessment for case-control studies can entirely eliminate the uncertainty in identifying past individual exposures to these six CAHs. The records for such an accurate assessment typically do not exist, or they are limited to a minority of workplaces, so that historical exposure assessments must inevitably rely on expert judgment to a large degree in most cases. The methodologic challenge, therefore, is to develop approaches which can improve the validity and reliability of such judgments and thus the interpretation of causal associations in epidemiologic studies. The development of these approaches deserve increased critical attention in the literature.

In this context, the key objective of this effort was to develop a matrix with features which would improve the accuracy of estimating past exposures. The combination of these features in one matrix has not been reported before. The probability and intensity scales were introduced in order to allow stratification and analysis of trends by both scales. The rationale is that etiologic inferences would be stronger if the risk estimates increased with increasing intensity of cumulative exposure within the same probability strata and with increasing probability in each stratum of cumulative exposure.

Another feature of the matrix is the use of decade indicators to ensure that exposure assignments result only for those decades when a CAH was likely used in a given industry or occupation. The results of the application of the matrix to a case-control data set suggest that this feature reduced misclassification, because the matrix designated a smaller proportion of the industries as entailing multiple exposures at any particular time than would have been the case with fixed assignments covering the entire period of the study. No effort was made to account for temporal change of exposure intensities in jobs or industries, although such an approach might have been fruitful.

Finally, the matrix described in this report can be used as a screening mechanism to identify specific job-industry combinations for which additional efforts to obtain information about putative exposures might be attempted. Such additional information could help reduce the number of false positive exposure assessments, which is critical, because false positive assignments are the most important contributors to the dampening of risk estimates through misclassification when the exposure prevalence is low [Stewart et al., 1991]. At least in theory, this approach would also be quite cost-effective, because it would be limited to a small number of jobs. A limited effort to seek additional information for a small group of jobs was made in this study, but it did not prove successful.

Other methodologic issues also arise from the specific characteristics of the matrix. First, the proportion of study subjects designated as exposed, illustrated in Table V, are quite high, in the range of 15–40% for the different CAHs (when including all probabilities). In contrast, the overall proportions of subjects exposed to the same CAHs in a population followed in Montreal are much smaller, in the range of 1–4% [Siemiatycki et al., 1991]. The latter proportions are closer to those assigned high probabilities by our matrix. Our study population had been purposefully selected from areas with a high proportion of petrochemical and other industrial workers, among whom exposure to the six CAHs may be more common than in Montreal, and this may account for some of the difference in the estimated proportions of exposed subjects. A more likely explanation, however, is simply that our matrix is very sensitive but with low specificity for the low and medium exposure probabilities. These characteristics of the matrix, however, should produce only nondifferential misclassification, which would tend to mask possible causal relationships by moving risk estimates toward the null and dampening exposure-response gradients [Copeland et al., 1977; Stewart et al., 1991; Blair et al., 1990].

A number of specific approaches to the use of the matrix are described in this report, including the use of a cumulative exposure score as the surrogate of dose, the precise manner of its calculation, and the ways in which probability assignments are combined with intensity estimates from industry and job to calculate cumulative exposure scores. These approaches are reflected in the algorithm, and they seem reasonable to the authors, but they are by no means the only or the "best" possible approaches. Their rigid or mechanical application would be a mistake. Indeed, the use of alternative methods to estimate surrogate measures of dose and to combine matrix parameters to explore potential risks may also be reasonable [Blair et al., 1990]. Indeed, one of the objectives of the matrix design was to keep the individual elements distinct so that different summary approaches could be applied.

Finally, the automatic combination of estimates of probabilities and intensities of exposure which the matrix assigned independently for industry and occupation deserves a word of caution because it can produce false positives. For example, truck drivers (SOC code 6413) were initially treated as a Category B occupation, because exposures are better defined by the industry in which the typical tasks for this occupation are performed (i.e., only truckers in an industry *likely to handle* one of the CAHs as their cargo would be exposed). The automatic procedure of the matrix, however, incorrectly assigned exposure to all truck drivers in industries with CAH use (dry cleaning, agriculture, metal machinery, etc.) where the cargo would almost certainly not be a CAH. To correct this problem, a new SOC code was introduced to assign only those truck drivers carrying chemicals as a Category A occupation. All other truck drivers were considered unexposed. The modified SOC codes which were developed in this manner are unique to the exposures of interest in this study.

Despite these methodologic concerns and study-specific details, the matrix described in this report is potentially applicable to other case-control or register-linkage studies where the occupations and industries are coded according to the four-digit SIC and SOC systems. The matrix also has the potential for future improvement in its specificity if more detailed information can be obtained about the historical use and the resulting probabilities and intensities of exposure to these CAHs in various jobs and industries.

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